IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

OREXO AB and OREXO US, INC.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C.A. No. 14-829 (SLR) (SRF)
	)	
ACTAVIS ELIZABETH LLC,	)	
	)	
Defendant.	)	

OREXO'S OPENING CLAIM CONSTRUCTION BRIEF

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I. BACKGROUND

Plaintiffs, Orexo AB and Orexo U.S., Inc. (collectively, "Orexo") develop new medicines by applying innovative drug delivery technologies to drug substances. Orexo's Zubsolv® employs patented technology in sublingual tablets used to treat adults addicted to opioid drugs.

Zubsolv® contains two active ingredients, buprenorphine and naloxone. Buprenorphine is an opioid analgesic used to treat different types of pain. In "substitution therapy" buprenorphine is used to aid patients in the recovery from dependence on other opioids like heroin. But buprenorphine-containing pharmaceutical formulations are themselves potential targets for drug abuse. Patients solubilize the active ingredient in conventional formulations and inject it. To address this, naloxone, an opioid antagonist that reverses the effects of opioid analgesics, was added to the formulations. But these formulations remain susceptible to abuse.

The scientists at Orexo developed Zubsolv®, an abuse-resistant buprenorphine/naloxone formulation for sublingual administration. Significantly, the Zubsolv® formulation reduces the amount of active ingredient by over 25% while achieving the same pharmacologic effect as previously known buprenorphine/naloxone tablets. Zubsolv® is based on innovative drug delivery technologies claimed in several patents: U.S. Patent No. 8,454,996 ("the '996 patent"), U.S. Patent No. 8,470,361 ("the '361 patent"), U.S. Patent No. 8,658,198 ("the '198 patent"), and U.S. Patent No. 8,940,330 ("the '330 patent"). The '996 and '330 patents are at issue in this litigation.

The '996 patent claims a method of sublingually administering a tablet comprising (1) microparticles of buprenorphine, "presented at" (claim 1) or alternatively "adhered to" (claim 2) the surfaces of carrier particles, and (2) a bio/mucoadhesion promoting agent also in a mixture with carrier particles. (JA09, '996 pat., col. 12, lines 18-43). By incorporating a bio/mucoadhesion promoting agent, the active ingredient stays near the mucosal surface under

the tongue and sublingual absorption is improved. The family tree for the '996 patent is provided at JA34.[1]

The '330 patent claims tablets for sublingual administration comprising (1) microparticles of buprenorphine on carrier particles, where the buprenorphine is in contact with particles comprising citric acid, and also contains (2) naloxone, and (3) certain disintegrants. (JA33, '330 pat., col. 24, lines 17-31). The claimed formulation increases buprenorphine bioavailability by over 25%, allowing for a reduced amount of opioid available for abuse by addicts. (JA27-28, '330 pat., col. 12, line 56 – col. 13, line 23). The '330 patent also claims methods of manufacturing such formulations. (JA33, '330 pat., col. 24, lines 48-60).

II. CLAIM CONSTRUCTION GENERALLY

Claim construction addresses how persons of ordinary skill in the art ("skilled persons") understand the patent claim language, based on the claims, patent specification, and file history. The claims provide substantial guidance on the meaning of claim terms and the correct construction stays true to the claim language. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-14 (Fed. Cir. 2005). The specification and file history provide further guidance. *Id.* at 1315. Courts may also consult extrinsic evidence to understand the science and meaning of claim terms based on the relevant art. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S.Ct. 831 (2015).

III. CONSTRUCTION OF DISPUTED '996 PATENT CLAIM LANGUAGE

Orexo's claim constructions rely on the intrinsic evidence and Dr. Nicholas A. Peppas's Declaration addressing how skilled persons understand the patent claims. Dr. Peppas, a member

[1] Citations to "JA" refer to the Joint Appendix to be filed when claim construction briefing is complete.

of the National Academy of Engineering, has over 30 years of experience in pharmaceutics. See Peppas Decl. ¶¶ 3-24 and Ex. A (Curriculum Vitae)[2].

Orexo also refers to claim constructions adopted by the New Jersey District Court in *Orexo v. Mylan*, C.A. No. 11-3788, 2014 WL 1302056 (D.N.J. Mar. 31, 2014). (JA3180-3217). That Court construed claim language in U.S. Patent No. 6,761,910 ("the '910 patent"), the grandparent to the '996 patent (and part of the patent family covering Orexo's platform technology for sublingual formulations). See JA34.

For the '996 patent, the parties dispute the constructions for three claim phrases: (A) "carrier particles" (claims 1, 2), (B) "***presented at*** the exterior surfaces of the carrier particles" (claim 1 only), and (C) "effective amount" (claim 2).[3] The two '996 patent claims with the disputed phrases highlighted are provided below:

Claim 1:

> A method comprising sublingual administration to an individual of a pharmaceutical composition in the form of a tablet sized for placement under a tongue, wherein the composition comprises
> (a) water-soluble ***carrier particles*** having exterior surfaces,
> (b) microparticles of buprenorphine or a pharmaceutically-acceptable salt thereof, wherein said microparticles are smaller than the ***carrier particles*** and are admixed with the ***carrier particles***, and
> (c) particles of a bioadhesion and/or mucoadhesion promoting agent consisting essentially of a polymer that swells when brought into contact with saliva, admixed with the ***carrier particles***,
> wherein the microparticles of buprenorphine or a pharmaceutically-acceptable salt thereof are ***presented at the exterior surfaces of the carrier particles***.

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[2] "Peppas Decl." refers to the June 11, 2015 Declaration of Dr. Nicholas A. Peppas on Claim Construction for U.S. Patent Nos. 8,454,996 and 8,940,330.

[3] On February 18, 2015, Actavis asserted that all three phrases were indefinite. (JA3232-34, Actavis's Invalidity Contentions, pp. 28-29, 62). In the March 6 Court ordered exchange of claim terms and proposed constructions, Orexo provided constructions for all phrases; Actavis provided a construction for one. (JA3237-40, Orexo's list of terms; JA3244, Actavis's list of terms). Actavis proposed constructions for the remaining phrases the day before the '996 patent Joint Claim Construction Statement was due.

(JA09, '996 pat., col. 12, lines 18-34) (emphasis added).

Claim 2:

> A method comprising sublingual administration of at least one dosage unit of an essentially water free pharmaceutical composition to an individual, said pharmaceutical composition comprising an ***effective amount*** of buprenorphine or a pharmaceutically-acceptable salt thereof in the form of microparticles adhered to the surfaces of ***carrier particles*** which are substantially larger than said microparticles and are essentially water-soluble, and a bioadhesion and/or mucoadhesion promoting agent.

(JA09, '996 Pat., Col. 12, lines 35-43) (emphasis added).

A. "Carrier particles" ('996 Patent Claims 1, 2) (Peppas Decl. ¶¶ 32-48)

Orexo's Proposed Construction	Actavis's Proposed Construction
March 6 exchange: In the context of the claims, particles comprising one or more pharmaceutically acceptable substances, ***at or near*** the surfaces of which may be other particles.	Feb. 18: indefinite March 6 exchange: none presented March 26: ***Pre-formed*** particles comprising one or more pharmaceutically acceptable substances, ***attached to*** the surfaces of which are other particles.

Orexo's construction adopts the plain meaning of "carrier particles" as understood by persons of ordinary skill in the art. (Peppas Decl. ¶¶ 32-41). Actavis initially did not provide a construction, asserting indefiniteness. (JA3232, Invalidity Contentions, p. 28). Actavis then used Orexo's construction, but added the requirements that (1) other particles be ***attached*** to the carrier particles and (2) that the carrier particles be "***pre-formed***," a process limitation. Actavis's add-ons (for non-infringement purposes) do not convey how skilled persons understood "carrier particles."

The '996 Patent Claim Language. The '996 patent claims describe a product that comprises carrier particles, microparticles of buprenorphine or a salt thereof, and a bio/mucoadhesion promoting agent. (JA09, '996 pat., col. 12, lines 18-43). The claims address

the size (e.g., substantially larger), and placement (e.g., presented at) of carrier particles relative to other components of the claimed composition. The claims also describe properties of the carrier particles (e.g., "water-soluble"). (JA09, '996 pat., col. 12, lines 18-43).

Claim 1 states "microparticles of buprenorphine…are ***presented at*** the exterior surfaces of the carrier particles." (JA09, '996 pat., col. 12, lines 18-33) (emphasis added). In contrast, claim 2 uses the words "buprenorphine…in the form of microparticles ***adhered to*** the surfaces of carrier particles"). (JA09, '996 pat., col. 12, lines 34-43) (emphasis added). The use of different language in different claims highlights that the relationship between carrier particles and other particles in the claimed formulation can vary as emphasized by the different language in claims 1 and 2. (See Peppas Decl. ¶¶ 35, 46-48). The claims do not use Actavis's words "pre-formed" or "attached" and the language "pre-formed" is found nowhere in the intrinsic record.

The '996 Patent Specification. The '996 specification states that the carrier particles may be ***any*** pharmaceutically acceptable substance:

> ***The carrier used may comprise any substance which is pharmaceutically acceptable***, is highly soluble in water, and which can be formulated into particles fit for incorporating a bio/mucoadhesion promoting agent.

(JA05, '996 pat., col. 4, lines 41-45) (emphasis added); Peppas Decl. ¶¶ 37-38. The specification then lists some materials that may be used as carriers, and that they may incorporate a bio/mucoadhesion promoting agent. (JA05, '996 pat., col. 4, lines 46-49). The specification also discloses preferred amounts of carrier particles in relation to bio/mucoadhesion promotion agent and preferred sizes for the carrier particles. (JA05, '996 pat., col. 4, lines 22-27, 37-62).

The specification describes the relationship between carrier and other particles, demonstrating that other particles may be at or near the surfaces, but are not always "attached to" the carrier particles (the word "attached" itself does not appear in the specification). For

example, the specification refers to "carrier substances" "coated" with active agents (JA05, '996 pat., col. 3, lines 36-38), describes a bio/mucoadhesion agent "positioned at" the exterior surfaces of carrier particles (JA06, '996 pat., col. 5, lines 57-60), and includes a preferred embodiment with particles of a bio/mucoadhesion promoting agent "adhered to" the surfaces of carrier particles (JA06, '996 pat., col. 5, lines 62-67). Actavis's construction ignores these alternatives and the patentee's express use of different terms that differentiate the patent claims and alternative embodiments. (Peppas Decl. ¶¶ 39, 46-48).

"Carrier particles" would thus be understood by a person of ordinary skill in the art as "particles comprising one or more pharmaceutically acceptable substances, at or near the surfaces of which may be other particles." (Peppas Decl. ¶ 32). Any additional characteristics of the carrier particles (e.g., water solubility, relative size) and their placement in the final formulation are described by other language in the claims. (JA09, '996 pat., col. 12, lines 18-43; Peppas Decl. ¶¶ 33-34, 43).

The '996 Patent Prosecution History. The prosecution history removes any doubt on this point. ***Claim 1 was expressly amended to remove "adhered to" and insert the language "presented at."*** (JA2022, '996 File History, 02/22/2013 Amendment, p. 3). "Carrier particles" appears in both claim 1 (presented at) and claim 2 (adhered to). Therefore, the construction for "carrier particles" must permit particles to be "presented at" without the requirement that they be "adhered to" the surfaces to stay true to the claim language. Actavis's construction overlooks this express distinction. (Peppas Decl. ¶¶ 41, 46-48).

Actavis's construction ignores the express language of the claims ("presented at"), the alternatives in the specification (disclosing "positioned at" in addition to "coated"), and the express removal of the language ("adhered to") during prosecution (see above).

Actavis also improperly reads "pre-formed" into the claim language "carrier particle." Skilled persons understand that the "carrier particles" referred to are in the claimed pharmaceutical composition, and the claims do not require more. (Peppas Decl. ¶¶ 43-45). The claims do not contain the language "pre-formed." And the specification explains that carrier particles may be "any substance which is pharmaceutically acceptable." (JA05, '996 pat., col. 4, lines 41-45). This language does not place any limitation on when or how the carrier particles are formed. The '996 patent provides examples of suitable carriers (JA05, '996 pat., col. 4, lines 46-49), and how to manufacture carrier particles that may comprise a bio/mucoadhesion promoting agent (JA05, '996 pat., col. 4, lines 6-9; col. 6, lines 3-27) or a fragmentation promoting agent (JA05, '996 pat., col. 4, lines 50-52). But the specification emphasizes that these examples are not limiting. (JA09, '996 pat., col. 12, lines 11-16 ("the invention is not limited to these examples and embodiments…The scope of the invention is thus only limited by the appended claims); JA07, '996 pat., col. 8, lines 1-3 ("…reference to examples showing preferred but not limiting embodiments.")).

The prosecution history also shows Actavis's construction is wrong. First, in the reasons for allowance of the grandparent '910 patent, the examiner highlighted that the '910 patent claims (which, like the '996 claims address a method of treatment using the novel composition) relate to a "quickly dissolvable dosage form" with a "structural difference" from the prior art. (JA235, '910 File History, Notice of Allowability, p. 2). Second, during prosecution of the '215 application (parent to the '996 patent), the examiner emphasized that the claims were product claims and were not limited to a mixing process. (JA722-23, '215 App. File History, Sept. 10, 2007 Office Action, pp. 6-7); *Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370,

1372-73 (Fed. Cir. 2000) ("A novel product that meets the criteria of patentability is not limited to the process by which it was made.").

Finally, when addressing other claim terms in the grandparent '910 patent, the New Jersey Court in *Orexo v. Mylan* confirmed that the composition claims are not limited to a specific manufacturing process. (JA3191-92, NJ '910 Opinion, pp. 12-13).

B. "Presented at the exterior surfaces of the carrier particles" ('996 Patent Claim 1) (Peppas Decl. ¶¶ 49-64)

Orexo's Proposed Construction	Actavis's Proposed Construction
March 6 exchange: Positioned at the outside part or layer of the carrier particles.	Feb. 18: indefinite March 6 exchange: Admixed for a sufficiently long time to cover the outside part or layer of a pre-formed carrier particle. March 26: Admixed for a sufficiently long time to cover ***or affix to*** the outside part or layer of a pre-formed carrier particle.

Orexo's construction ("positioned at") adopts the plain meaning of the term mandated by the intrinsic evidence and adopted by the New Jersey Court when construing a related patent. Actavis first asserted that "presented at" was indefinite; then dropped that position and provided two constructions, eventually asserting that the active be "admixed for a sufficiently long time to cover or affix to … a pre-formed carrier particle." Actavis's changing constructions ignore the plain meaning of the claim language, imports process limitations into claim language that unquestionably addresses position/placement, and again reads the language "pre-formed" into the claims. (pp. 6-7).

The '996 Patent Claim Language. The plain meaning of the phrase "presented at" is "positioned at." (Peppas Decl. ¶¶ 49-50). In contrast (as explained above), claim 2 uses the

phrase "adhered to" to convey the concept of something being "attached." Use of different words in the claims connotes different meanings. *CAE Screenplates v. Heinrich Fiedler GmbH*, 224 F.3d 1308, 1317 (Fed. Cir. 2000).

The New Jersey Court in *Orexo v. Mylan* construed "presented at" to mean "positioned at;" not "adhered to" in Orexo's related U.S. Patent No. 8,512,747 ("the '747 patent")" (JA3219, 06/27/2014 Markman Hearing Tr., 50:7-12: "Well, I'm not going to adopt the 'adhered to' because I do agree it's different. I will use the term 'positioned at.' I don't need more argument on that. 'Positioned at' will be the definition in the construction that I will give to the term.").[4]

The '996 Patent Specification. The specification confirms that "present" and "positioned" are used interchangeably (and mean the same thing):

'996 Pat., col. 4, lines 6-9	'996 Pat., col. 5, lines 57-60
"The bio/mucoadhesion promoting agent must then be ***present on the surface*** of the carrier particles, but it may optionally also be present within these particles, as described below."	"In order for the pharmaceutical composition of the invention to function properly when a bio/mucoadhesion promoting agent is added thereto, this agent must be ***positioned at the surfaces*** of the carrier particles."

(Peppas Decl. ¶¶ 53). Skilled persons understand by reading the specification that "presented at" means "positioned at." (Peppas Decl. ¶¶ 53, 58).

The '996 Patent Prosecution History. As addressed above (p. 6), during prosecution claim 1 was amended to remove the "adhered to" language and replace it with "presented at" (JA2022, '996 File History, 02/22/2013 Amendment, p. 3) emphasizing that the two phrases have different meanings. Actavis's construction ignores the express claim language "presented at" and substitutes "to cover or affix" in its place. Actavis improperly inserts attachment

[4] The '747 and '996 patents are related. (JA34). Claim 1 in both patents has the language "presented at." '996 patent claim 2 and '747 patent claim 3 use the phrase "adhered to." (JA09,'996 pat., col. 12, lines 32, 40; JA3179, '747 pat., col. 12, lines 31, 42).

requirements into the claims (e.g., affixed or covered) even though Orexo ***expressly*** removed language of attachment (adhered to) and replaced it with language of location (presented at).

Actavis's construction improperly inserts an unidentified amount of mixing time and an unspecified amount of "coverage" of carrier particles into the claim phrase "presented at." But, the word "admixed" is used elsewhere in the claim, and would not be understood to be part of the phrase "presented at." (Peppas Decl. ¶ 57). And, while the specification does provide non-limiting examples of mixing times (see e.g. JA06-07, '996 pat., col. 5, lines 62-67 ((mixed together for a "sufficient time"); col. 7, lines 12-14 (addressing one possible active ingredient, fentanyl)), they should not be read into claim language that does not address mixing, coverage or affixation, but instead addresses location. Other portions of the specification show that "presented at" addresses position and support the claim language. (Peppas Decl. ¶¶ 53, 58).

Actavis's construction also incorrectly imports the terms "to cover or affix" into the phrase "presented at." Neither claim requires Actavis's undisclosed amount of "coverage." (Peppas Decl. ¶ 60). And, as addressed above (pp. 5-6), the specification provides different relationships between the carrier particles and other components of the formulation. While the phrase "presented at" overlaps with some of those relationships, it is different and should be given its plain meaning. (Peppas Decl. ¶ 61). The prosecution history (amending "adhere" to "presented at") further confirms the distinction between the phrase "presented at" and the concept of particles that are adhered or affixed to other particles. Actavis's construction eliminates that distinction.

And again, other portions of the file history (in addition to the express removal of "adhered to" in claim 1 and insertion of "presented at") confirm that the claims address structure and location of the product at issue. As mentioned above (p. 7), in the grandparent '910 patent

prosecution, the examiner's reasons for allowance highlight by reference to "present on the surface" that the claims address location and structural product features: "The invention of the ['910 patent] claims…are novel over the prior art in that they provide a quickly dissolvable ***dosage form***, where the mucoadhesives are ***present on the surface***…This ***structural difference*** provides the major difference and improvement over other delivery methods." (JA235, '910 File History, Notice of Allowability, p. 2) (emphasis added). Also, as previously addressed, during prosecution of the U.S. Patent Application 10/851,215 (parent to the '996 patent), the applicant explained that the structure of the final product was different than the prior art, and relied on the differences in the manufacturing processes to support that statement. (JA508, '215 App. File History, June 12, 2007 Response to Office Action, p. 9). In his response the examiner highlighted that, "The claims are drawn to a product comprising components, not a method mixing components to form a product." (JA722-23, '215 App. File History, Sept. 10, 2007 Office Action, pp. 6-7).

Actavis originally alleged that the phrases "presented on the surfaces of carrier particles" and "carrier particles" were indefinite. Eventually, Actavis landed on its current construction requiring "admix[ing] for a sufficiently long time," and pre-forming of carrier particles and that other particles "cover" or be "affixed to" the carrier. Actavis's changing positions in the face of the plain meaning of the language, the intrinsic evidence, and the New Jersey Court's construction show that Actavis's constructions are litigation driven and not based on the intrinsic record or understanding of skilled persons.

C. "Effective amount" ('996 Patent Claim 2) (Peppas Decl. ¶¶ 65-68)

Orexo's Proposed Construction	Actavis's Proposed Construction
March 6 exchange: An amount ***capable of conferring*** a desired therapeutic response or effect. March 26 proposed compromise: An amount that ***elicits a (i.e., is capable of conferring*** a desired) therapeutic response or effect.	Feb. 18: Not addressed in '996 patent, but phrase using "pharmacologically-effective amount" in '198[5] patent indefinite March 6 exchange: none presented March 26: An amount that elicits a therapeutic response.

In *Orexo v. Mylan*, addressing the '910 grandparent patent, Orexo proposed and the New Jersey Court agreed that "effective amount" means "an amount that elicits a therapeutic response." (JA3215-17, NJ '910 Opinion, pp. 36-38). Orexo pointed out, and the Court recognized, that the '910 patent (with the same disclosure as the '996 patent on this point) teaches that the invention is intended to "giv[e] rise to pharmacologically effective plasma levels" of an active agent (JA04, '996 pat., col. 2, lines 36-41), but does not equate "pharmacologically effective" with a particular end result. (JA3216, NJ '910 Opinion, p. 37).

Actavis originally alleged that the phrase "pharmacologically-effective amount of an opioid analgesic" in the '198 patent was indefinite despite the New Jersey Court's previous construction for "effective amount" (JA3234, Actavis's Invalidity Contentions, p. 62). To resolve any doubt in the New Jersey Court's construction as a result of Actavis's contentions, Orexo added the explanation that "elicits" is understood to mean "capable of conferring." This definition is expressly provided in the '330 patent (addressed below) and the '198 patent (no longer at issue in this case):

> The term "pharmacologically effective amount" refers to an amount of an active ingredient, which is ***capable of conferring a desired therapeutic effect*** on a treated patient…
>
> (JA26, '330 pat., col. 9, lines 30-32) (emphasis added).

[5] The parties resolved the portion of the case addressing the '198 patent.

The added language emphasizes that the specification teaches that the invention is intended to ("capable of") "giv[e] rise to pharmacologically effective plasma levels" of an active agent. (JA04, '996 pat., col. 2, lines 36-41; JA3215, NJ '910 Opinion, p. 36; Peppas Decl. ¶¶ 65-68).

IV. CONSTRUCTION OF DISPUTED '330 PATENT CLAIM LANGUAGE

Orexo's claim constructions for the '330 patent also rely on the intrinsic evidence and Dr. Peppas's Declaration addressing how skilled persons understand the patent claims, the intrinsic evidence and the technology.

For the '330 patent, the parties dispute the constructions for five claim phrases: (A) "carrier particles" (claims 1, 3-6, 10), (B) "***presented upon*** the surface of carrier particles" (claim 1), (C) "pharmacologically-effective amount" (claim 1), (D) "in contact with" (claim 1), and (E) "not in the same particle" (claim 1).[6] Independent claim 1 of the '330 patent with the disputed phrases highlighted is:

Claim 1:

> A tablet composition suitable for sublingual administration comprising:
> microparticles of a ***pharmacologically-effective amount*** of buprenorphine, or a pharmaceutically-acceptable salt thereof, ***presented upon the surface of carrier particles***, wherein microparticles of buprenorphine or a pharmaceutically acceptable salt thereof are ***in contact with*** particles comprising citric acid, wherein the buprenorphine or pharmaceutically acceptable salt thereof and the citric acid are ***not in the same particle***;

[6] On June 4th, Actavis withdrew its contention that "particles of citric acid" (in claim 6 only) is indefinite and agreed that it would not be raised in the parties' respective briefs. (JA3266, June 4 e-mail). Accordingly, the claim term is no longer disputed and should be construed as the "particles comprising citric acid" that are referred to in independent claim 1 (Orexo's proposed construction). (JA3264, May 28 Joint Cl. Const. St., p. 4). The '330 patent specification describes an embodiment that illustrates claim 6, "water soluble carrier particles may also comprise the weakly acidic, and/or weakly acidic buffer forming materials, mentioned herein before (such as citric acid and/or sodium citrate)." (JA25, '330 pat., col. 7, lines 32-35).

a ***pharmacologically-effective amount*** of naloxone, or a pharmaceutically-acceptable salt thereof; and
a disintegrant selected from the group consisting of croscarmellose sodium, sodium starch glycolate, crosslinked polyvinylpyrrolidone and mixtures thereof.

(JA33, '330 pat., col. 24, lines 17-31) (emphasis added).

A. "Carrier particles" ('330 Patent Claims 1, 3-6, 10) (Peppas Decl. ¶¶ 69-84)

Orexo's Proposed Construction	Actavis's Proposed Construction
(Same as '996 patent) May 20 exchange: In the context of the claims, particles comprising one or more pharmaceutically acceptable substances, at or near the surfaces of which may be other particles.	May 20 exchange: A pre-formed particle upon the outside part or layer of which is ***affixed*** other particles. May 28: Pre-formed particles ***comprising one or more pharmaceutically acceptable substances***, ***attached to*** the surfaces of which are other particles.

The parties' dispute here mirrors the dispute addressed for "carrier particles" in the '996 patent above (pp. 4-8). Since the '330 patent is not part of the same family of patents as the '996 patent, the intrinsic record differs ***but still supports*** Orexo's construction for "carrier particles." And the support in both patent families shows that Orexo's construction is how skilled persons understand the reference to carrier particles.

Actavis initially presented a claim construction for "carrier particles" in the '330 patent that was different from its claim construction for the same language in the '996 patent. (JA3259, May 20 list of terms). Approximately one week later, Actavis modified its construction for the '330 patent to bring it in line with its previous construction for the '996 patent. Actavis's changing positions regarding the construction shows that their positions are not driven by the intrinsic evidence or understanding of skilled persons.

The '330 Patent Claim Language. '330 patent claim 1 requires the presence of carrier particles and describes their position in the claimed composition in relation to other components.

(JA33, '330 pat., col. 24, lines 17-32). As in the '996 patent claims, the relationship between carrier particles and other particles is described by other language in the claims ("presented upon the surface" in claim 1). (Peppas Decl. ¶¶ 69-70).

Dependent claims 3-6 describe preferred substances that may comprise the carrier particles (e.g., water soluble substances, mannitol, citric acid), and preferred size of the carrier particles. (JA33, '330 pat., col. 24, lines 35-44). Claim 10 is a process claim that provides one possible way to make the claimed pharmaceutical composition. (JA33, '330 pat., col. 24, lines 54-56). These claims demonstrate that any properties of carrier particles, their position relating to other materials, and how they are incorporated into the composition are described by other language in the claims, and are not built into the meaning of "carrier particles" by itself. (Peppas Decl. ¶¶ 71-72).

The '330 Patent Specification. The '330 patent specification describes carrier particles:

> ***Carrier particles may comprise pharmaceutically-acceptable substances*** that are soluble in water, such as carbohydrates… Alternatively, ***carrier particles may comprise pharmaceutically-acceptable substances*** that are insoluble or sparingly soluble in water…"

(JA25, '330 pat., col. 7, lines 28-45) (emphasis added); Peppas Decl. ¶ 73. The specification also lists some materials that may be used as carriers, and preferred sizes for carrier particles. (JA25, '330 pat., col. 7, lines 28-45; col. 7, line 60 – col. 8, line 24; col. 7, lines 23-27). (Peppas Decl. ¶ 74).

As with the '996 patent, the '330 specification describes the relationship between the carrier and other particles, highlighting that other particles may be at or near the surfaces, but not always "attached to" the carrier particles. For example, the specification refers to particles of naloxone that may be "presented upon the surfaces of, and/or between, carrier particles" (JA25, '330 pat., col. 8, lines 44-46), and disintegrant that may be "presented, at least in part, as

particles upon the surfaces of, and/or between, carrier particles" (JA25, '330 pat., col. 8, lines 51-54). (Peppas Decl. ¶ 75). The specification also describes a preferred, non-limiting embodiment with "a[n] interactive mixture comprising at least one population of carrier particles upon the surfaces of which are presented (e.g. adhered) microparticles of buprenorphine or a pharmaceutically acceptable salt thereof." (JA24-25, '330 pat., col. 6, line 66 – col. 7, line 4). This embodiment, which includes an interactive mixture, is a preferred non-limiting embodiment, as demonstrated by the use of "e.g." in "presented (e.g. adhered)." The "e.g." demonstrates that it is one, but not the only, example of the relationship between particles in the formulation. As Dr. Peppas explains, a skilled person would understand that "adhered" is a subset of the broader language "presented at." (Peppas Decl. ¶ 76); *Black's Law Dictionary* (9th ed. 2009) ("e.g." is the short form of *exempli gratia*, which means "for example.").

"Carrier particles" would thus be understood by skilled persons as "particles comprising one or more pharmaceutically acceptable substances, at or near the surfaces of which may be other particles." (Peppas Decl. ¶ 69). Any additional characteristics of the carrier particles (e.g., water solubility, composition, size) and placement in the final formulation are addressed in other language in the claims and specification. (Peppas Decl. ¶¶ 70-71).

The '330 Patent Prosecution History. The prosecution history supports the plain meaning of the phrase "carrier particles." The examiner's amendment to claim 1 (original claim 24) added the phrase "presented upon the surface of carrier particles." (Compare JA3019, '330 File History, Nov. 4, 2014 Examiner's Amendment to Claim 24, p. 2 with JA2981, '330 File History, Sept. 18, 2014 Amendments to the Claims, Claim 24, p. 2). A person of ordinary skill in the art would understand from this added language that the relationship between carrier

particles and other materials is described by other words in the claim and not by the phrase "carrier particles" itself.

Actavis's construction is wrong for the same reasons addressed in the '996 patent. The relationship between carrier particles and other particles is not defined by the phrase "carrier particles" itself, but by other claim language and by reference to the specification which provides positional information that is not limited to only situations where there is adherence. (Peppas Decl. ¶¶ 75-80). Actavis's incorporation of the term "affixed" into its May 20 construction and changing it to "attached to" one week later underscores that Actavis's addition of both terms is not supported by the intrinsic evidence.

Actavis's construction also incorrectly imports the word "pre-formed" into the construction for carrier particles. The '330 patent claims 1-7 claim pharmaceutical formulations, and do not require "pre-forming" of carrier particles. The examiner focused on the structure of the tablet in allowing the patent, highlighting that the claimed tablet "exhibits unexpectedly superior sublingual buprenorphine bioavailability due to the ingredients as well as the ***structural characteristics*** recited in the instant claims." (JA3022, '330 File History, Nov. 4, 2014 Notice of Allowability, p. 5) (emphasis added). When applicants sought claims for a process of manufacture, they expressly did so, as shown by process claims 8-11 through language that expressly identifies the claims as process claims, not through the phrase "carrier particles." (Peppas Decl. ¶¶ 82-83).

B. "Presented upon the surface of carrier particles" ('330 Patent Claim 1) (Peppas Decl. ¶¶ 85-97)

Orexo's Proposed Construction	Actavis's Proposed Construction
(Same as '996 patent) May 20 exchange: Positioned at the outside part or layer of the carrier particles.	May 20 exchange: ***Affixed to*** the outside part or layer of carrier particles.

As with the '996 patent (pp. 8-11), the dispute here centers on the words "presented upon." Orexo's construction adopts the plain meaning of the claim language. As explained by the New Jersey Court: "presented" simply means "positioned." (p. 9). This language has the same meaning in the '330 patent and the '996 patent. (Peppas Decl. ¶¶ 85-86).

Actavis again improperly reads requirements into its construction for "presented," but advocates for different requirements for the same term in the '996 and '330 patents ('996 patent: "admixed for a sufficiently long time to cover or affix to"; '330 patent: "affixed to"). Actavis's inconsistent constructions ignore the plain meaning of the claim language, import an additional process limitation into the '996 patent but not the '330 patent, require more than position by reading an affixation requirement into the language "presented upon," and again read the language "pre-formed" into the claims through its construction for "carrier particles." (pp. 9-11).

The '330 Patent Claim Language. Claim 1 of the '330 patent claims a pharmaceutical formulation where microparticles of buprenorphine or a pharmaceutically-acceptable salt thereof are "presented upon the surface of carrier particles." Nothing in claim 1 suggests anything but the plain meaning of "presented."

The '330 Patent Specification. The specification uses the phrase "presented upon" / "presented on" without deviating from the ordinary meaning (e.g., "presented on" (JA25, '330 pat., col. 7, lines 57-59), weakly acidic materials that "may be presented, at least in part, upon the

surfaces of, and/or between, carrier particles" (JA25, '330 pat., col. 8, lines 25-28), and naloxone that "may also be presented upon the surfaces of, and/or between, carrier particles" (JA25, '330 pat., col. 8, lines 44-47)). It does not require that it is affixed or attached. In each of these instances, the term "presented upon" / "presented on" refers to placement or positioning of the referenced materials. As another example, the specification describes that buprenorphine and other materials "are presented in associative admixture with each other," meaning that they are positioned such that at least some of the material is in contact with, but not necessarily attached to another material. (JA24, '330 pat., col. 6, lines 46-65). (Peppas Decl. ¶¶ 87-88).

The specification also refers to an alternative where buprenorphine microparticles "***may*** be presented in the form of ***interactive mixtures*** with carrier particles" (JA25, '330 pat., col. 8, lines 35-40). As previously addressed on pp. 15-16, interactive mixtures are preferred, non-limiting embodiments with adherence between particle surfaces. (Peppas Decl. ¶¶ 76, 89).

A skilled person, reviewing the specification, including the non-limiting alternatives in the specification would understand that "presented upon" is not limited to affixed or attached, but is used consistently with its plain meaning, "positioned at."

The '330 Patent Prosecution History. The examiner's amendment added the claim 1 language "presented upon the surface of carrier particles." (Compare JA3019, '330 File History, Nov. 4, 2014 Examiner's Amendment to Claim 24, p. 2 with JA2981, '330 File History, Sept. 18, 2014 Amendments to the Claims, Claim 24, p. 2). The examiner explained, "Applicant has demonstrated the unexpected result that when similar components are formulated according to the instant invention such that microparticles of buprenorphine, or a pharmaceutically-acceptable salt thereof are presented upon the surface of carrier particles…" (JA3021, '330 File History, Nov. 4, 2014 Notice of Allowability, p. 4; Peppas Decl. ¶ 90). This demonstrates that the

language "presented upon the surface of carrier particles" should be given its plain meaning without the additional limitations proposed by Actavis.

Actavis's different constructions of essentially the same language in the '996 and '330 patents emphasize the arbitrary nature of the limitations that Actavis imposes on the claims through construction. Actavis's differing constructions for the two patents are repeated below:

Claim Language	**Actavis's Construction**
'996 patent: presented at the exterior surfaces of the carrier particles	***admixed for a sufficiently long time*** to ***cover or affix*** to the outside part or layer of a pre-formed carrier particle.
'330 patent: presented upon the surface of carrier particles	***affixed*** to the outside part or layer of carrier particles

While Actavis includes "admixed for a sufficiently long time to cover or affix" in its construction for the '996 patent, it does not include that limitation in its construction of essentially the same language in the '330 patent instead requiring only that it be "affixed." As addressed above (pp. 10-11), the "affixed" language that Actavis incorporates into both constructions is not supported by the intrinsic evidence. The term "affixed" does not appear anywhere in the specification. In addition, consistent with Orexo's construction (and contrary to Actavis's construction), the terms "presented upon" / "presented on" are used throughout the specification without requiring that the "presented" materials be "affixed." (Peppas Decl. ¶¶ 94-95).

C. "Pharmacologically-effective amount" ('330 Patent Claim 1) (Peppas Decl. ¶¶ 98-101)

Orexo's Proposed Construction	Actavis's Proposed Construction
May 20 exchange: An amount that ***elicits a (i.e., is capable of conferring*** a desired) therapeutic response or effect.	Feb. 18: phrase using "pharmacologically-effective amount" in '198 patent indefinite May 20 exchange: none presented May 27: An amount that ***elicits*** a therapeutic response.

As noted above, Actavis initially alleged that the phrase "pharmacologically-effective amount of opioid antagonist" in the '198 patent was indefinite despite being aware of the New Jersey Court's construction of "effective amount" as "an amount that elicits a therapeutic response" and despite the express language in the '198 patent specification, which is also found in the '330 patent specification at issue here. (pp. 11-12).

The '330 Patent Specification. The '330 (and '198) patent specifications provide express language that further explains "pharmacologically-effective amount" and resolves any ambiguity that Actavis may allege in the New Jersey Court's construction:

> The term "pharmacologically effective amount" refers to an amount of an active ingredient, which is ***capable of conferring a desired therapeutic effect*** on a treated patient…
>
> (JA26, '330 pat., col. 9, lines 30-32) (emphasis added).

The specification also explains that pharmacologically-effective amounts are "capable of producing, and/or contributing to the production of, the desired therapeutic effect…" (JA26, '330 pat., col. 9, lines 37-40). These express explanations in the patent specifications eliminate any dispute, explain the term "elicits," and are consistent with the New Jersey Court's construction. (Peppas Decl. ¶¶ 98-101).

D. "In contact with" ('330 Patent Claim 1) (Peppas Decl. ¶¶ 102-107)

Orexo's Proposed Construction	Actavis's Proposed Construction
May 20 exchange: Touching at least in part. "In contact with" includes the presence of quickly dissolving coatings on one or other, or both, sets of particles.	May 20 exchange: "wherein microparticles of buprenorphine or a pharmacologically-acceptable salt thereof are ***in contact with*** particles comprising citric acid, wherein the buprenorphine or pharmaceutically acceptable salt thereof and the citric acid are ***not in the same particle***" is indefinite

The phrase "in contact with" should be given its ordinary meaning, as understood by skilled persons, which is "touching at least in part" and that it may include "the presence of quickly dissolving coatings on one or other, or both, sets of particles." (Peppas Decl. ¶ 102).

The '330 Patent Claim Language. The '330 patent claims use the phrase "in contact with" consistent with its plain meaning.

The '330 Patent Specification. The '330 patent specification defines "in contact with" as particles that are "at least in part, in intimate contact with each other. This includes the possibility of the inclusion of quickly dissolving coatings on one or other, or both, sets of particles." (JA24, '330 pat., col. 6, lines 58-65; Peppas Decl. ¶ 103).

The '330 Patent Prosecution History. The '330 prosecution history confirms that the phrase "in contact with" should be accorded its plain meaning and is understood by persons of ordinary skill in the art. During prosecution, applicant amended the claim language "intimate contact" to remove the word "intimate," making the claim "in contact with particles…" (JA2981, '330 File History, Sept. 18, 2014 Amendment to claim 24). Applicant explained that "by deleting the term 'intimate' the claim language presently recites that the 'microparticles of a pharmacologically-effective amount of buprenorphine, or a pharmaceutically-acceptable salt thereof, [are] in contact with particles comprising citric acid'. ***This is intended to have its plain meaning***." (JA2984, '330 File History, Sept. 18, 2014 Remarks, p. 5) (emphasis added). That

plain meaning is provided in the specification portion quoted above. (Peppas Decl. ¶¶ 103-105). The examiner, recognized as a matter of law to be a person skilled in the art, understood the language and permitted its presence in the claims. *In re Lee*, 277 F.3d 1338, 1345 (Fed. Cir. 2002) (examiners are presumed to act from skilled person's viewpoint).

Dictionary definitions also support the plain meaning of "in contact with." (JA3225, *Collins Dictionary* (10th ed. 2009), p. 368 ("the act or state of touching physically"); JA3229 *The American Heritage High School Dictionary* (4th ed. 2010), p. 308 ("the state or condition of touching or of immediate proximity")). (Peppas Decl. ¶ 106).

Actavis's assertion that the claim 1 language using the phrase "in contact with" is indefinite is contradicted by the definition in the specification, the prosecution history and the plain meaning of the phrase. (Peppas Decl. ¶¶ 102-107).

E. "Not in the same particle" ('330 Patent Claim 1) (Peppas Decl. ¶¶ 108-112)

Orexo's Proposed Construction	Actavis's Proposed Construction
May 20 exchange: "Not in the same" means in a different. "Particle" means small piece or fraction.	May 20 exchange: "wherein microparticles of buprenorphine or a pharmacologically-acceptable salt thereof are ***in contact with*** particles comprising citric acid, wherein the buprenorphine or pharmaceutically acceptable salt thereof and the citric acid are ***not in the same particle***" is indefinite May 27: "Not in the same" means in different, but language above indefinite

The language "not in the same particle" should be given its ordinary meaning: "not in the same" means "in a different" and "particle" means "small piece or fraction." Put together, the phrase means "in a different small piece or fraction." Actavis originally asserted in its May 15, 2015 contentions that the phrase above (with highlighting provided by Actavis) was indefinite. It repeated its contention in the May 20 exchange of claim constructions (again providing the

same highlighting). Although (on May 27) Actavis belatedly agreed that "not in the same" means "in different," it alleges that the entire claim phrase remains indefinite.

While the term "particle" is understood by persons of ordinary skill in the art, Orexo construes it here as a result of Actavis's indefiniteness contentions. The plain meaning of "particle" is "small piece or fraction." (JA3226, *Collins Dictionary* (10th ed. 2009), p. 1205 ("an extremely small piece of matter"); JA3230 *The American Heritage High School Dictionary* (4th ed. 2010), p. 1014 ("a very small piece or part; a tiny portion or speck")). (Peppas Decl. ¶¶ 109-111).

The '330 Patent Prosecution History. The '330 prosecution history confirms that the phrase "not in the same particle" is not indefinite (as Actavis contends) and would be understood by a person of ordinary skill in the art. This language was added to the claims in an examiner's amendment. (Compare JA3019, '330 File History, Nov. 4, 2014 Examiner's Amendment to Claim 24, p. 2 with JA2981, '330 File History, Sept. 18, 2014 Amendments to the Claims, Claim 24, p. 2). The examiner also contrasted prior art that "results in a sublingual tablet comprising particles no larger than 800 microns,[7] and ***containing buprenorphine and citric acid within the same particle***" with the invention of the '330 patent where "microparticles of buprenorphine, or a pharmaceutically-acceptable salt thereof are presented upon the surface of carrier particles, and

[7] Actavis originally asserted that "microparticles" in the '996 patent meant "a mean particle size of less than 10 µm" and in the '330 patent meant "particles with a weight mean diameter between about 0.5 µm and about 15 µm, but in any event smaller than any carrier particle" despite overwhelming evidence in favor of Orexo's construction. (JA3249, Mar. 27 Joint Cl. Const. St., p. 4; JA3259, May 20 list of terms). For example, Actavis's construction was rejected by the New Jersey Court, was based on expressly non-limiting preferred embodiments in the patent specifications and a dependent claim of the '330 patent, and contrary to the examiner's statement in the '330 file history that particles in the 400-500µm range are microparticles. (JA3207-10, NJ '910 Opinion, pp. 28-31; JA2969, '330 File History, July 22, 2014 Office Action p. 5). On May 27, Actavis abandoned its constructions and agreed to Orexo's construction for both patents, namely "particles in the 1 to 1000 micrometers (microns) range." (JA3262-63, May 28 Joint Cl. Const. St., pp. 2-3).

are in contact with particles comprising citric acid, and wherein the ***buprenorphine or pharmaceutically acceptable salt thereof and the citric acid are not in the same particle***." (JA3021, '330 File History, Nov. 4, 2014 Notice of Allowability, p. 4) (emphasis added); Peppas Decl. ¶ 112. The examiner's use of this language "not in the same particle" and 'in contact with" and consideration of the amendment of the claims demonstrate that the phrase is not indefinite and is understood by persons of ordinary skill in the art. *In re Lee*, 277 F.3d at 1345 (examiners are presumed to act from skilled person's viewpoint).

V. CONCLUSION

As addressed above, Orexo's claim constructions are the only proposals supported by the intrinsic and extrinsic evidence and should be adopted.

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June 11, 2015

CERTIFICATE OF SERVICE

I hereby certify that on June 11, 2015, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on June 11, 2015, upon the following in the manner indicated:

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